UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/471,523	12/23/1999	Richard B. van Breemen	21726/90386	7519

23644 7590 09/09/2004

BARNES & THORNBURG
P.O. BOX 2786
CHICAGO, IL 60690-2786

EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/471,523	VAN BREEMEN ET AL.	
	Examiner	Art Unit	
	MY-CHAU T TRAN	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-30* is/are pending in the application.

4a) Of the above claim(s) *24-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-23 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 December 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Applicant's response filed 6/23/04 is acknowledged and entered.

2. Claims 1-5 and 7-12 were canceled by the amendment filed on 12/3/03.

3. Claim 6 was canceled by the amendment filed on 3/5/02.

4. Claims 13-30 are pending.

Election/Restrictions

5. This application contains claims 24-29 are drawn to an invention nonelected with traverse in Paper filed 6/25/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

6. This application is a divisional of PCT/US99/11,493 filed 5/25/1999, which claims priority to a provisional application 60/086,813 filed 5/26/1998.

7. Claims 13-23 and 30 are treated on the merit in this Office Action.

Maintained Rejections

Claim Rejections - 35 USC § 112

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 13-23, and 30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (This is a written description rejection)

The instant claim 13 recites a high throughput method for screening a compound of interest comprising the steps of 1) placing a solution of biological material that has a higher molecular weights than the compound of interest into an ultrafiltration chamber. The chamber comprises a membrane with a pore size that does not allow the biological material to pass through; 2) Placing the compound of interest into the ultrafiltration chamber, which comprises a membrane with a pore size that does allow passage of the compound; 3) Providing a continuous flow of a supportive solution to the ultrafiltration chamber that facilitates the reaction between the compound and biological material; 4) The product produce by the reaction would pass through the membrane, and the product is structurally and/or functionally different from the compound of interest; 5) The product is analyzed to determine whether the compound is suitable for use as a drug or natural product.

The specification disclosure does not sufficiently teach the presently claimed screening method because, firstly, the claimed screening method would require prior knowledge of the

characteristics of both reactants (i.e. the biological material and the compound of interest) since the biological material must be of higher molecular weight than the known compound so that the biological material would not pass through the membrane. For example, if the biological material is a protein and the compound is a known drug, the claimed screening method would have required prior knowledge of the characteristics of both the protein and the known drug such that the protein has a higher molecular weight. The specification is directed to the screening method of the reaction in which cytochromes P450 metabolized the drug, wherein the drug includes imipramine, chlorpromazine, and pentoxyresorufin (pg. 10, line 11 to pg. 11, line 2). The specification example 1 discloses the method of screening for the oxidized form of chlorpromazine due to the hepatic cytochromes P450 oxidation of chlorpromazine. Example 2 discloses the method of screening for the oxidation product of pentoxyresorufin by cytochrome P450 2B-catalyzed O-dealkylation activity. Thus the specification does not sufficiently teach the relationship between biological materials and known compounds to use in the claimed high throughput screening method.

Secondly, since prior knowledge of both reactants in a reaction is required for the claimed screening method then the product of the reaction would also be known. Thus the claimed screening method is screening for a product that is already known, wherein its use would be apparent.

Thirdly, the claimed analyzing step requires the extrapolation of the resulting analyses of the reaction product to determine the use of the compound as a drug or natural product. The specification is silent on how the product is being analyzed in order to determine that the compound can be used as a drug or natural product. Thus the specification does not sufficiently

teach how the product is being analyzed in order to determine that the known compound can be used as a drug or natural product.

The specification is directed to the screening method for the interaction of cytochromes P450 (biological material) and a drug (compound of interest), wherein the drug includes imipramine, chlorpromazine, and pentoxyresorufin. These methods clearly do not provide an adequate representation regarding the relationship between all biological materials and known compounds for the claimed screening method. The specification's examples are drawn specifically to the interaction of cytochromes P450 with the drug such as imipramine, chlorpromazine, and pentoxyresorufin. Thus the specification does not teach the claimed high throughput screening method.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of the screening method of the reaction in which cytochromes P450 metabolized the drug, wherein the drug includes imipramine, chlorpromazine, and pentoxyresorufin disclosed by the specification, the skilled artisan cannot envision the method of screening that would require prior knowledge of the relationship between any reactants (i.e. the biological material and the compound) and the analysis step wherein the resulting analyses of the product of the reaction would determine the use of the compound as a drug or natural product.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the specification support the screening method of the reaction in which cytochromes P450 metabolized the drug, wherein the drug includes imipramine, chlorpromazine, and pentoxyresorufin. The specification does not teach the presently claimed high throughput screening that would require prior knowledge of the relationship between any reactants (i.e. the biological material and the compound) and the analyses step wherein the resulting analyzes of the product of the reaction would determine the use of the compound as a drug or natural product. Therefore, only the screening method of the reaction in which cytochromes P450 metabolized the drug, wherein the drug includes imipramine, chlorpromazine,

and pentoxyresorufin, but not the full breadth of the claim method would meet the written description provision of 35 U.S.C 112, first paragraph, but not the full breadth of the presently claim high throughput screening method.

10. Claims 13-23, and 30 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: 1) the step of determining how the product is structurally and/or functionally different from the initial compound of the reaction. The step is required in order to provide a membrane that would only allow the "product" to pass through to form the second solution.

2) The step wherein the resulting analysis of the product of the reaction would determine the use of the compound as a drug or natural product. This step(s) is essential in order to extrapolate the analysis of the product to determine that the compound of interest can be use as a drug or natural product.

3) The step of analyzing the product of the reaction when the products are small molecules that are absorbed by the cell as claimed in claim 21. The step is required in order to provide a membrane that would only allow the "product" to pass through to form the second solution.

4) The step of extrapolating the concentrations of the small molecules to determine cellular permeability or absorption as claimed in claim 30 for the determination of the compound for use as a drug or a natural product. This step(s) is essential in order to extrapolate the analysis of the product to determine that the compound of interest can be use as a drug or natural product.

Response to Amendment

11. The declaration under 37 CFR 1.132 filed 6/23/04 is sufficient to overcome the rejection of claims 13-22 based upon the rejection under 35 U.S.C. 102(a) as being anticipated by van Breemen et al. (*Drug Metabolism and Disposition*, **2/1998**, 26(2):85-90).

Withdrawn Rejections

12. The rejection of claims 13-22 under 35 USC 102(a) as being anticipated by van Breemen et al. (*Drug Metabolism and Disposition*, **2/1998**, 26(2):85-90) has been withdrawn in view of the filed declaration under 37 CFR 1.132.

Response to Arguments

13. Applicant's arguments directed to the rejection under 35 U.S.C. 112, first paragraph (written description), for claims 13-23, and 30 have been fully considered but they are not persuasive for the following reasons.

Applicant contends that the presently claimed invention is clearly defined by the specification because 1) "*The written description requirement is satisfied by the applicant's disclosure of such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention. Put another way, one skilled in the art, reading the original disclosure, must reasonably discern the limitation at issue in the claims. Crown Operations Int'l, LTD v. Solutia Inc., 289 F.3d 1367, 2002 (Fed. Cir., May 13, 2002, Decided) Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQZd 1961, 1966 (Fed. Cir. 1997)*". 2) "*The purpose of the "adequate written description requirement" is to ensure that the inventor*

had possession of the claimed subject matter at the time the application was filed. If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met. In re Alton, 76 F.3d 1 168, 1996 U.S. App. LEXIS 1691 (Fed. Cir., February 5, 1996, DECDED). 3) "*Compliance with the written description requirement is essentially a fact-based inquiry that will necessarily vary depending on the nature of the invention claimed.'" Enzo Biochem, 296 F.3d at 1324, 63 USPQZd at 1613. The present invention is for a general method and does not require demonstrating all possible uses.*"

Applicant's arguments are not convincing since the presently claimed method is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

1) It is the examiner position that applicant's disclosure has not met the written description requirement such that the claimed invention is fully set forth because the presently claimed method is "*A high throughput method for determining whether a known compound or a mixture of compounds is suitable for intended use as a drug or a natural product*", i.e. testing known compounds, which are ***not*** known as a drug or a natural product, to see if it can be a drug or a natural product. The specification disclosure and examples is directed to a screening method of the reaction in which cytochromes P450 metabolized drug wherein the drug includes imipramine, chlorpromazine, and pentoxyresorufin (see specification pg. 10, line 11 to pg. 11, line 2; Example 1 and 2), i.e. testing known compounds, which are already known as drug. Thus

applicant's disclosure has not met the written description requirement such that the claimed invention is fully set forth. Additionally, the case laws cited by applicant, i.e. *Crown Operations Int'l, LTD v. Solutia Inc.* and *Lockwood v. American Airlines, Inc.* are not applicable to the written description rejection since they are regarding prior art issues.

2) Applicant cited case law of *In re Alton* with regard to written description rejection, however *In re Alton* is referring to the whether rebuttal evidence is sufficient to overcome the prima facie case of obviousness. Thus it is unclear how this is applicable to the written description rejection.

3) It is the examiner position that although "*the present invention is for a general method*" it does require that a representative number of possible uses should be demonstrated, i.e. an adequate number of species is require in order to support the claimed genus. Thus the presently claimed method does require that a representative number of possible uses should be demonstrated.

Accordingly, the rejection under 35 U.S.C. 112, first paragraph (written description), is hereby maintained.

14. Applicant's arguments directed to the rejection under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps for claims 13-23, and 30 have been fully considered but they are not persuasive for the following reasons.

Applicant alleges that "*the examiner has overlooked the first few words in Section 2172.01 which states "(a) claim which omits matter disclosed to be essential to the invention as described in the specification or in other statements of record may be rejected...." The steps*

stated in the rejection as having been omitted are not "disclosed" in our specification as essential and there are no statements of record that such steps are essential."

Applicant's arguments are not convincing since the steps stated in the rejection are essential steps of the claimed method. MPEP 2172.01 states, "*In addition, a claim which fails to* ***interrelate essential elements*** *of the invention as defined by applicant(s) in the specification may be rejected under 35 U.S.C. 112, second paragraph, for failure to point out and distinctly claim the invention.*" The specification on page 7 discloses, "*The pore sizes of the membrane are selected based on the size of the predetermined resulting compounds or molecules and biological material*" (lines 2-3). Thus since the steps stated in the rejection are essential steps of the claimed method.

Accordingly, the rejection under 35 U.S.C. 112, second paragraph as being incomplete for omitting essential steps is hereby maintained.

Conclusion

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MY-CHAU T TRAN whose telephone number is 571-272-0810. The examiner can normally be reached on Mon.: 8:00-2:30; Tues.-Thurs.: 7:30-5:00; Fri.: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANDREW WANG can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

mct
September 3, 2004

ANDREW WANG
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600